

nous literature attests to its importance among the symptoms of cardiovascular disease. Toxins have been shown to be etiologic in arteriosclerosis and kidney disease, and it is most likely that focal infections do play a rôle in the production of hypertension. Cholesterol, as an etiological factor, demands much more investigation. Excessive food proteins have been considered for a long time irritating to the kidneys and, more recently, as distinct disturbers of the acid-base balance. Of the three outstanding theories for the production of hypertension, as mentioned by Doctor Nuzum, focal infections and excessive food proteins appear to be factors, perhaps acting separately or conjointly, in the writer's opinion. However, for the study of many of our problems we wish to make animal investigations. Several years ago the writer studied the effects of adrenalin injections in rabbits and found arteriosclerosis. We apparently prevented its development by using coincidentally potassium iodide. At that time we did not seriously differentiate the so-called spontaneous or natural arteriosclerosis of rabbits from the experimentally induced type. This differentiation has been well noted by Nuzum in the study of his lesions. In contrast with some of the other investigators, Nuzum has been mindful of well-balanced diets and has studied a liberal number of animals including controls. The coronary sclerosis in his liver-fed animals is a good reproduction of the human type, and was not found in our experimental work. Furthermore, he has produced pathology with evidences similar to human cardiovascular and renal disease, viz., hypertension, acid urine, albuminuria, cylindruria, decreased carbondioxide content of the blood plasma and other signs of retention, such as increased blood urea nitrogen and nonprotein nitrogen. This is indeed a formidable array of evidence.

The writer considers that this is a most interesting and valuable experimental study and hopes that the work may be continued. A study of the activity of bacterial and food proteins separately and conjointly in experimental vascular pathology as to quantitative results might prove of value.

NEWTON EVANS, M. D. (Loma Linda, California)—Some of the questions about arterial hypertension, kidney damage, and arteriosclerosis are elucidated by Doctor Nuzum's study. It presents much food for thought, but it is evident that much of the problem is still unsolved. His clear presentation of the differences between the endarteritis apparently resulting from the abnormal diet and the spontaneous medial arterial changes in rabbits is convincing.

His main contention that *atherosclerosis* is directly related to the disturbance of the acid-base equilibrium of the body, particularly on the acid side, seems consistent with the observations on the animals used. What the real relationship between morphological kidney changes, arteriosclerosis and high blood pressure are, is still apparently far from settled. Since his observations seem to indicate that in all three groups of animals fed upon abnormally high protein rations there were seen *high blood pressure and signs of nephritic changes* irrespective of whether the animal was overacid or overalkaline, one might still be justified in suspecting that the high protein is in some way responsible for these effects.

If the acid-base equilibrium disturbance could be experimentally maintained without the use of excessively high protein ration, the result might give information of a more conclusive nature on the point stressed by Nuzum.

One cannot but feel that perhaps conclusions would be more valuable if an animal such as the rat, whose dietary apparently more nearly resembles that of man, were used as was done by McCollum and his associates, as well as by Risley and me, in observing the effects of high protein upon kidney structure and function.

A. M. MOODY, M. D. (Saint Francis Hospital, San Francisco)—I believe that Doctor Nuzum has produced in his experimental rabbits an arteriosclerosis typical, grossly and microscopically, of that seen in man. This work also sets forth very clearly the differences between the spontaneous type of arteriosclerosis and the type artificially produced in rabbits. There is, however, much work still necessary to prove conclusively whether the changes present are the result of a disturbance of the acid-base

equilibrium or whether they are the result of the action of toxic substances produced somewhere by the improper splitting and subsequent disposition of the protein molecule after ingestion. This work would also tend to prove that there is some difference in the changes occurring in rabbits fed largely on vegetable protein and in those fed on animal protein. The determination of causes—of which there must be many—of arteriosclerosis is an enormous problem, and Nuzum's work presents important evidence of the association of an acid-base disturbance with arteriosclerosis and high blood pressure.

SUPERFICIAL EPITHELIOMATA

A REVIEW OF THE CASE HISTORIES OF PATIENTS
TREATED IN THE OUT-PATIENT DEPARTMENT OF
THE UNIVERSITY OF CALIFORNIA MEDICAL
SCHOOL BETWEEN 1920 AND 1926

By C. J. LUNSFORD AND LAURENCE TAUSSIG*

DISCUSSION by W. F. Howard Taylor, Los Angeles;
Douglass W. Montgomery, San Francisco.

THE material for this paper was drawn from 230 histories of patients applying to the clinic for treatment of basal and squamous-celled epitheliomata between 1920 and 1926. We have attempted to demonstrate, principally by means of tables, some of the instructive features revealed by a careful study of these histories. In many instances the records were not complete, and in many more the patients were lost sight of too early to judge the final result of treatment. We have emphasized the differentiation between basal and squamous-celled growths on account of the relative benignity of the first in comparison with the latter. Most of the patients whose records were reviewed were first seen and were treated in the dermatology clinic, though a number were referred to the surgical department. Of those treated in the skin clinic the greater number received radium therapy, often in conjunction with x-ray, curettage, cautery, desiccation or surgery. The number of patients is too small to compare the various methods of treating the different types of lesions and we have avoided making such comparisons.

AGE INCIDENCE

In Table I we have indicated the incidence of basal-celled and squamous-celled epitheliomata by decades. It will be noted that about 10 per cent of the squamous-celled growths occur before the age of 40, while only about 1 per cent of the basal-celled growths occur during this period. On the other hand, 30 per cent of the basal-celled new growths occurred after the 70th year; while only 21 per cent of the total number of the squamous type occurred at this time. It is of interest to note that the peak of the incidence in this series of skin and mucous

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Laurence R. Taussig (384 Post Street, San Francisco). M. D. University of California, 1918; A. B. and M. S. University of California. Present hospital connections: Instructor in dermatology, University of California. Scientific organizations: San Francisco County Medical Association, California Medical Association, American Medical Association. Practice limited to Dermatology since 1919.

TABLE I—According to AGE

YEARS	BASAL CELL		SQUAMOUS CELL	
	No.	%	No.	%
20-30.....	1	1.1	1	.7
31-40.....	0	0	13	9.2
41-50.....	12	13.7	22	15.6
51-60.....	23	24.1	41	29.
61-70.....	27	31.	34	24.1
71-80.....	20	23.	25	17.7
80 up.....	6	7.	5	3.5
TOTAL.....	89	100%	141	100%

membrane new growths occurs during the fifth and sixth decades, whereas the incidence of cancer in general is usually considered to be somewhat lower.

SEX INCIDENCE

Table II indicates that of the total basal and squamous-celled epitheliomata, 70 and 95 per cent, respectively, occur in men. The seven to three ratio of the basal-celled cases is in keeping with the usual understanding. Of the twenty cases of squamous-celled epitheliomata occurring on the glabrous skin three only occurred in women. Of the sixty-six lip epitheliomas three were in women. Of the twenty-three tongue carcinomas one was in a woman, and of the thirty-two mouth cancers, other than of the tongue, none occurred in women.

INCIDENCE ACCORDING TO LOCATION

The incidence of basal and squamous-celled growths according to the location of the lesion is indicated in Table III. It will be seen that on the face, other than the ear, the ratio of basal to squamous-celled lesions is six and one-half to one, while on the ear the ratio is reversed, being three and one-half squamous to one basal. This is in accordance with the usual statistics. One hundred per cent of the growths on the mucous membranes were squamous-celled in this series. Included under epitheliomata of the skin are several basal-celled growths which originated on the skin of the lips and later spread to the vermilion border, finally extending to the gum. Of the basal-celled epitheliomata of the face about 60 per cent were on the nose and cheek. Many of these involved the naso-labial fold and extended in all directions. Of the remainder about ten occurred near or at the inner canthi of the eyes, often extending to the eyelids and to the bridge of the nose.

DURATION BEFORE APPLYING FOR TREATMENT

Table IV is a graph of the basal and squamous-celled epitheliomata according to the limits of and average duration of time the lesions had existed at the time the patient first visited the clinic. Comparing the two it will be noted that of the basal-celled growths the extreme limits of time are three months and eighteen years with an average of four years, and that of the squamous-celled growths between three weeks and eight years with an average of thirteen months. This indicates the type of case our clinic receives for treatment and explains the relatively small number of cures we have obtained.

RESULTS OF TREATMENT OF EPITHELIOMATA OF THE GLABROUS SKIN

Table V shows that of all cases of basal-celled epitheliomata, a clinical cure has been obtained in 67 per cent. Closer analysis of the histories shows that of the cases of basal-celled epitheliomata applying for treatment during the first year, a clinical cure was obtained in 100 per cent. Those coming for treatment after a duration of five years or those who had received previous ineffective treatment were about twice as difficult to cure. The squamous-celled lesions which we apparently cured had a history of less than two years' duration.

In our tables "clinical cure" means freedom from symptoms for at least one year. "Question" means that the patient had not been under observation for a sufficient length of time to permit a correct estimate of the effects of treatment.

RESULTS OF TREATMENT IN SQUAMOUS-CELLED EPITHELIOMATA OF LOWER LIP

In Table VI we have classified the cases of squamous-celled epitheliomata of the lower lip into (1) those without demonstrable metastasis; (2) those with demonstrable metastasis; and (3) those regarded when first observed as being hopeless and which received palliative treatment only. Of those without demonstrable metastasis practically one-half were clinically cured at the time of their last visit. The period over which they were observed after healing is shown by glancing at the chart. Many of them have not been seen in months and some not in years; therefore, their ultimate fate is unknown. Nine out of forty-seven, however, were well after the lapse of a year. Seven did not respond favorably to treatment and presumably died of cancer.

Under "questionable cases" is included four patients in various stages of involvement referred to surgery and two referred to other hospitals. The

TABLE II—According to SEX

LOCATION	BASAL				SQUAMOUS			
	MALE		FEMALE		MALE		FEMALE	
	No.	%	No.	%	No.	%	No.	%
Face, other than lips and ear.....	61	67.8	26	29.9	11	7.9	2	1.4
Lips.....	0	0	0	0	63	43.9	3	1.4
Ear.....	2	2.3	0	0	6	4.7	1	.7
Tongue.....	0	0	0	22	16.6	1	.7
Mouth other than tongue.....	0	0	0	32	23.7	0	...
TOTAL.....	63	70.1%	26	29.9%	134	95	7	5%

TABLE III—According to LOCATION

	BASAL		SQUAMOUS	
	No.	%	No.	%
Face, other than ear...	87	87%	13	13%
Lip—lower.....	0	...	66	100%
Ear.....	2	22%	7	78%
Tongue.....	0	...	23	100%
Mouth, other than tongue.....	0	...	32	100%
TOTAL.....	89	39% of whole	141	61% of Whole

others were not under observation long enough to permit any estimate of results. Of the sixteen patients with demonstrable metastases one shows a four-year cure, five were worse under treatment, and ten did not return to the clinic for observation. The chart shows that the squamous-celled epitheliomata of the lip have a poor prognosis after metastasis has occurred.

RESULTS OF TREATMENTS OF EPITHELIOMATA OF THE MOUTH OTHER THAN THE TONGUE

In Table VII we have classified the patients into (1) those whose tumors were clinically localized; (2) those in whom the local growth was either extensive or in which there was a demonstrable metastasis; and (3) the hopeless. Of the eight patients with relatively localized tumors two show a two-year clinical cure and one a four-year clinical cure. Many of those listed under "extensive" were, in fact, hopeless from the beginning, and a clinical cure was obtained in none. Three improved and nine grew worse while under treatment, but were lost from observation before final results could be noted. The eight patients listed under "question" did not remain long enough under observation for complete treatment to be given.

It was not thought worthwhile to chart epitheliomata of the tongue. Nearly all such patients were far advanced when first observed. Many are listed as hopeless. A large number of them did not return after the first or second treatment and were thus lost sight of before the effects of treatment were known. Of the twenty-three patients studied one shows a five-year cure. The treatment was implantation of bare tubes of emanation in the local growth, followed by neck dissection. Nine grew worse under observation; nine did not remain under treatment long enough to permit of adequate observation; and four were listed as hopeless when first seen.

Summary—A study has been made of 230 cases of superficial epitheliomata. Separate analysis are made of the basal and squamous-celled types and of those of the skin and of the mucous membrane. Comparisons were based on age, sex, location, duration of time and primary end-results of treatment.

Results—Skin cases: Of the 109 skin cases 89 basal-celled epitheliomata show a 67 per cent cure, and 20 squamous-celled epitheliomata show a 55 per cent one to five-year cure.

Mucous Membrane Cases—Sixty-six squamous-celled epitheliomata of the lower lip show a 15 per cent one to four-year cure; 23 tongue cases show a 4 per cent five-year cure; and 32 mouth cases show a 9 per cent two to four-year cure.

CONCLUSIONS

The following conclusions are based on the data obtained from the tables:

(1) Squamous-celled epitheliomata of the skin occur at an earlier age than do basal.

(2) Men are two and one-third times as susceptible to basal-celled epithelioma and nineteen times as susceptible to squamous-celled epithelioma as are women.

(3) There are more basal than squamous-celled epitheliomata of the skin, excluding the ear. Most of the epitheliomata of the ear are squamous celled.

(4) Squamous-celled epitheliomata grow more rapidly and are more resistant to therapy than basal.

(5) A clinical cure is obtained in a larger proportion of basal-celled epitheliomata than in squamous.

(6) Patients having received previous treatment respond less rapidly to a subsequent treatment than untreated ones.

(7) The older a lesion is the more difficult it is to effect a cure, whatever the pathology.

(8) A successful result is very difficult to obtain in epitheliomata involving the mucous membrane.

DISCUSSION

F. W. HOWARD TAYLOR, M. D. (C. C. Chapman Building, Los Angeles) — A statistical paper that is honest, especially when dealing with a subject such as superficial epitheliomata, is a real contribution of present-day medicine and surgery. Sometimes claims of cures are made in discussion, or even in papers which, when analyzed, reveal either an improper diagnosis, a failure to classify the types of malignancy, or exaggeration on the part of the speaker.

Doctors Lunsford and Taussig should be congratulated on this unbiased paper which not only gives accurate tabulations, but shows application and work in its preparation. Wisely the preference of various forms of treatment has not been brought out, eliminating considerable useless argument. Contrary to the claims of some who are over-

TABLE IV—According to DURATION BEFORE APPLYING FOR TREATMENT

	BASAL		SQUAMOUS	
	LIMITS	AVERAGE	LIMITS	AVERAGE
Face other than ear.....	3 mo.—18 yrs.	4 yrs.	3 wks.—5 yrs.	2 yrs.
Lip.....	0	0	3 wks.—8 yrs.	13 mo.
Ear.....	2-4 yrs.	3 yrs.	8 mo.—1 yr.	10 mo.
Tongue.....	0	0	1 mo.—4½ yrs.	1 yr.
Mouth other than tongue.....	0	0	1 mo.—2 yrs.	10 mo.
AVERAGE TIME—for all.....		4 yrs.		13 mo.

TABLE V—According to RESULTS OF TREATMENT OF CANCERS OF GLABROUS SKIN

	BASAL						SQUAMOUS					
	CLINICAL CURE		RECURRENT		QUESTION		CLINICAL CURE		UNIMPROVED		QUESTION	
	No.	%	No.	%	No.	%	No.	%	No.	%	No.	%
Face, other than ear..	59	67%	17	19%	11	14%	7	54%	2	15½%	4	30½%
Ear.....	1	50%	1	50%			4	58%	2	28 %	1	14 %

TABLE VI—CARCINOMA OF LIP—RESULTS OF TREATMENT

	No.	CLINICAL CURE							WORSE	QUESTION
		3 Mo.	6 Mo.	9 Mo.	1 Yr.	1½ Yr.	2 Yr.	4 Yr.		
No Metastasis.....	47	9	5	1	1	3	4	1	7	16
Palpable Metastasis.....	16							1	5	10
Hopeless.....	3	Palliative Treatment								
TOTAL CASES.....	66									

TABLE VII—Shows RESULTS OF TREATMENT of the LESIONS IN MOUTH OTHER THAN TONGUE

	No.	CLINICAL CURE		IMPROVED	WORSE	QUESTION	DIED
		2 Yr.	4 Yr.				
Relatively localized.....	8	2	1	4		1	
Extensive.....	20			3	9	7	1
Hopeless.....	4						4

zealous for certain methods of handling these patients, this data will stand as an accurate guide to prognosis.

Most physicians who are treating squamous-cell epitheliomata even in its fairly early stage and without palpable metastasis are careful in treatment and are guarded in prognosis.

Eliminating the always present controversy of various methods of treating these lesions, there is nothing further I can add to this very complete and instructive paper.

DOUGLASS W. MONTGOMERY, M. D. (323 Geary Street, San Francisco)—The paper is an admirable estimate of cases in the experience of the authors themselves, and shows not only their experience, but also the good use they have made of their opportunities.

The division of epitheliomata into those that are squamous celled and those that are cuboidal celled is of more than academic interest, as the squamous-celled growths arise earlier in life, grow faster, and are more resistant to chemicals and to radiant energy than the cuboidal-celled ones. Because of their swifter growth, and the greater tendency to spread both locally and by metastasis, they are also more difficult to treat surgically. Another feature, however, of this cellular classification is that a particular growth may be not entirely one or the other, but may be mixed. It is only natural that this should be so, because the normal cells from which they all spring are not widely separated from one another, nor do they differ from one another very widely in their nature.

The subject of metastasis is important. An enlarged lymphatic nodule, even though adherent to the surrounding structures, and therefore not freely movable, and even if hard, and therefore indicating that it may be stuffed with dense hard epithelial cells, may be both indurated and attached because of inflammatory infiltration alone. Of course, the harder it is and the more immovable it is the likelier it is to be epitheliomatous, and when epitheliomatous infiltration has already extended as far as the neighboring lymphatic nodules the outlook for a cure is dark indeed.

The dangerous nature of these growths when situated on the auricle is justly referred to.

Of course, it is an important part of a well-rounded medical education that we should be aware of the difficulties of our occupation, but on the other hand it is not well that we should be too industrious in fabricating gloomy prognoses. If a steamship company should adver-

tise the dangers of the sea it would deter many from traveling. The statistics of nonsurgical treatment of cancer of the lip have of late years undergone a wonderful improvement, and even the very dangerous lesions of the mouth and tongue are, in some instances, not without hope, as these authors themselves have shown.

We have found in human life three most important factors in the production and control of its processes: (1) the application of energy of life from atoms; (2) the colloidal structure of the human protoplasm; and (3) the control exercised by the vegetative nervous system over these processes. These are the three great fundamental principles of life in the vertebrate, and a study of their action and deviation is necessary to the understanding of human vital processes. The control of the vegetative nervous system is largely in its action upon involuntary muscle, of which example is in the pupil of the eye, the heart, the muscles of our blood vessels (arteries, veins and capillaries). There are two kinds of muscles, voluntary and involuntary: the cerebrospinal system controls the voluntary. The latter is widely distributed in the human body, so that its control is most important. The capillaries of the circulatory system, where most of the interchange of substances with the blood goes on, have smooth muscles (called Houget cells) and, when it is considered that the capillaries in a small man have been estimated by Krogh at a total length of 62,000 miles, or two and a half times around the world, and their total area at 120,000 square yards, the influence of the vegetative nervous system in contracting and dilating these and its effect upon metabolism (or body processes), through this means alone, may be well appreciated. Its control over the heart, which normally pumps seven and one-half tons of blood a day, equivalent to lifting a ton of blood 122 feet high, is another example of its action.—Ellice McDonald, M. J. and Record.

A report of the tests recently made by the United States Public Health Service to determine the amount of danger involved from running a gasoline engine in a closed space states that a small twenty-three horse-power engine discharges one and a half cubic feet of carbon monoxide in a minute, or enough to poison the air of a closed garage, ten by twenty feet in size, to the danger point in about three minutes.—M. J. and Record.